

WHAT IS CLAIMED IS

1. An orally administrable composition containing nanoparticles with the particle size of 500 nm or less, comprising 0.1~30 weight% of a complex of a water-soluble drug and a counter-ion substance in which the charged water-soluble drug is bonded with the counter-ion substance, 0.5~80 weight% of a lipid, 0.5~80 weight% of a polymer, and 1~80 weight% of an emulsifier, wherein the weight ratio of said lipid and said polymer is in the range of 1:0.05~3.
2. The composition of Claim 1, wherein 70% or more of the water-soluble drug is entrapped in the nanoparticles.
3. The composition of Claim 1, wherein 80% or more of the water-soluble drug is retained in the presence of pancreatin.
4. The composition of Claim 1, wherein the water-soluble drug is a protein/peptide drug selected from the group consisting of insulin, erythropoietin, calcitonin, growth hormone, interferon, and somatostatin.
5. The composition of Claim 1, wherein the water-soluble drug is one charged in water selected from the group consisting of heparin, cepha antibiotic, sodium alendronate, sodium etidronate, and sodium pamidronate.

6. The composition of Claim 1, wherein the counter-ion substance is an anionic compound selected from the group consisting of sodium salt of C₈₋₁₈ fatty acid, sodium salt of bile acid, sodium alginate, sodium carboxymethylcellulose, and mixtures thereof.

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7. The composition of Claim 6, wherein the sodium salt of fatty acid is selected from the group consisting of sodium oleate, sodium lauryl sulfate, sodium caproate, and sodium laurate.

10 8. The composition of Claim 1, wherein the counter-ion substance is a cationic compound selected from the group consisting of carnitine salt, benzalkonium chloride, cetrimide, and mixtures thereof.

9. The composition of Claim 1, wherein the molar ratio of the water-soluble drug and
15 the counter-ion substance is in the range of 1:0.1~20.

10. The composition of Claim 9, wherein the molar ratio of the water-soluble drug and the counter-ion substance is in the range of 1:3~10.

20 11. The composition of Claim 1, wherein the weight ratio of the lipid and the polymer is in the range of 1:0.2~1.

12. The composition of Claim 1, wherein the lipid is an aliphatic alcohol selected from the group consisting of monoglyceride, diglyceride, propyleneglycol fatty acid ester, glycerol fatty acid ester, cetostearyl alcohol, cetyl alcohol, and mixtures thereof.

5 13. The composition of Claim 1, wherein the polymer is selected from the group consisting of methacrylic acid copolymer, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate phthalate, shellac, chitosan, hydroxypropyl methylcellulose and its derivative, ethylcellulose, methylcellulose, polyvinylalcohol, sodium alginate, carbomer, and mixtures thereof.

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14. The composition of Claim 1, wherein the emulsifier is selected from the group consisting of polyoxyethylene polyoxypropylene copolymer, polyethyleneglycol alkyl ether, polyoxyethylene castor oil, polyoxyethylene sorbitan fatty acid ester, transesterification product of natural vegetable oil triglyceride and polyalkylene polyol,
15 glycerol fatty acid ester, vitamin E polyethyleneglycol succinate, lecithin, sodium lauryl sulfate, bile acid and its derivative, and mixtures thereof.

15. The composition of Claim 1, further comprising 50 weight% or less of a solubilizing agent.

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16. The composition of Claim 15, wherein the solubilizing agent is selected from the group consisting of C₁₋₈ alcohol, dimethylsulfoxide, dichloromethane, toluene,

propyleneglycol, polyethyleneglycol, and 12-hydroxystearate.

17. The composition of Claim 1, further comprising 0.1~30 weight% of a cryoprotective agent.

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18. The composition of Claim 17, wherein the cryoprotective agent is selected from the group consisting of glucose, mannitol, sorbitol, trehalose, amino acid, albumin, and mixtures thereof.

10 19. The composition of Claim 1, wherein the particle size of the nanoparticles is in the range of 20~300 nm.

20. A method for preparing the orally administrable nanoparticle composition of Claim 1, comprising the steps of:

15 (a) ionically bonding a charged water-soluble drug with a counter-ion substance to form a complex of the water-soluble drug and the counter-ion substance;

(b1) adding a lipid, a polymer and a solubilizing agent to the complex obtained from step (a) and dissolving them, and adding the obtained solution to an aqueous solution containing an emulsifier, to obtain a homogeneous liquid phase, or

20 (b2) adding a lipid and a solubilizing agent to the obtained complex and dissolving them, and adding the obtained solution to an aqueous solution containing a polymer and an emulsifier, to obtain a homogeneous liquid phase; and

(c) eliminating the solubilizing agent from the mixture obtained from step (b1) or (b2).

21. The method of Claim 20, further comprising step (d) of minimizing the particle
5 size using a microfluidizer.

22. The method of Claim 20, wherein the charged water-soluble drug is obtained by treating the water-soluble drug with a pH adjusting agent to confer charge thereon in step (a).

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23. The method of Claim 22, wherein the pH adjusting agent is selected from the group consisting of hydrochloric acid, phosphoric acid, carbonic acid, citric acid, sodium hydroxide, sodium/potassium monohydrogen phosphate, sodium/potassium dihydrogen phosphate, sodium phosphate, sodium citrate, and mixtures thereof.